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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,939	05/11/2001	Hiroshi Yanagawa	2001-0580A	7033

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,939	YANAGAWA ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-28* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 15-26* is/are withdrawn from consideration.

5)☒ Claim(s) *27, 28* is/are allowed.

6)☒ Claim(s) *1,3,4,6,7 and 14* is/are rejected.

7)☒ Claim(s) *5 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicants' amendment in response to office action dated November 4, 2003 filed on May 4, 2004 is acknowledged. References Tucker et al., and Collinet et al. attached to the 'Amendment and Reply' are acknowledged. Claim 2 has been canceled. Claims 1, 3-5, 7-9, 11, 12 and 14 have been amended and entered. New claims 27 and 28 have been added. Therefore, claims 1 and 3-28 are currently pending and are under examination.

Response to Remarks and arguments

Election/Restriction:

Applicants have pointed out the inconsistency in the Office Action summary in PTOL 326 and the statement at page 2 of office action. It should be noted that there is an error in PTOL 326. The summary should be read as claims pending: 1-26; claims withdrawn from Examination: 9-13, 15-26; claims rejected: 1-8, 14, which has consistency with the statement at page 2 of the Office Action. Applicants request as to examining claim 9 along with the elected inventions has been considered but not found persuasive because the amended claim recites binding protein is an aryl hydrocarbon receptor and the reporter protein is alkaline phosphatase. Therefore, since the reporter protein alkaline phosphatase is a non elected species, claim 9 is withdrawn from further consideration. Applicants made an election without traverse and claims examined on merits are 1, 3-8, 14, 27 and 28 claims without traverse

Priority Date

The objection to claiming the filing date of November 11, 1998 of parent Japanese application 10/320102 as the priority date is withdrawn in view of Applicants' providing an English translation of the parent application.

Rejections under 35 USC § 112, Second Paragraph

The rejection of claims 1-8 under 35 USC § 112, second Paragraph is withdrawn in view of the amendment to the claims.

Rejections under 35 USC § 102

The rejection of claims 1-4 and 6 under 35 USC § 102 is withdrawn in view of the response and remarks on page12-13 of 'Amendment and Reply', and in view of the English translation of the priority document.

Objection to Claims

Claims 3-4 are/remain objected to as to including non-elected species. However, to advance the prosecution, claims will be treated in the light of the Restriction Election. Therefore, only hormone receptor will be examined from claim 3 and green fluorescent protein will be examined from claim 4.

Claims 5 and 8 are/remain objected to as to including non-elected species.

Claim 14 is/remains objected to as for depending upon non-elected claim. It is incumbent upon applicant to properly amend the claims.

Applicants arguments at page 8 as to pursuant to MPEP 820, a reasonable number of additional non-elected species be examined along with the elected invention have been considered but not found persuasive because pursuant to MPEP 820, where a genus is allowed, applicant may prosecute a reasonable number of additional species thereunder, in accordance with 37 CFR 1.141. The product claim as amended is not found allowable, therefore additional non-elected species claims are not under examination.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 6 and 7 are/remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a specific set of sensor proteins comprising a fusion protein composed of a reporter protein and a binding protein; does not reasonably provide enablement for all the sensor proteins composed of any binding proteins and any receptor proteins and fragments or mutants generated from any position located on the sequence of the sensor protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The invention includes a sensor protein comprising a fusion protein composed of a reporter protein and a binding protein, wherein said binding protein is inserted into the amino acid sequence of said reporter protein (claim 1), wherein the binding protein is a hormone receptor protein or a fragment thereof (claim 3), wherein the reporter protein is a green fluorescent protein or a mutant thereof (claim 4, 6, 7). The specification, however, only discloses cursory conclusions (see page 3, 8, 9, 18,), without data to support the findings. See the discussion below.

In response Applicants urge that current amendment overcomes the concern with regard to the binding protein by removing the mutant language and by adding the functional limitation that the fragments retain the ability of producing a change in the sensor protein upon binding to a target substance. It should be noted that as to the binding protein amended claim recites binding protein is 100-1000 amino acid residues in length, however, the specification fails to provide the positions in the sequence, which are critical to the protein's structure/function relationship, such as sites or regions directly involved in binding and activity.

As for the reporter protein variants Applicants argue at page 9 that mutants for the reporter protein are so well known that one of skill in the art can make and use them without undue experimentation. The arguments are not persuasive because specification does not provide a generic or a specific description as to the position in the amino acid sequence of the reporter protein which can generate a measurable signal when a binding protein or a fragment thereof is inserted therein.

In addition Applicants argue (page 10) that the specification provides working examples of numerous sensor proteins, which exemplify and enable the full scope of the claims, for

instance Examples 1 and 2 at page 25 and Example 3 at page 31. Applicants arguments have been considered but not found persuasive because the sensor protein exemplified in Example 1 and 2 comprises a fusion protein composed of a binding protein, Beta-lactamase and a reporter protein, Green Fluorescent Protein (GFP) and the sensor protein in Example 3 comprises a fusion protein composed of a binding protein, aryl hydrocarbon (Ah) receptor and a reporter protein, alkaline phosphatase. It should be noted that the binding protein Beta-lactamase in Example 1&2 and reporter protein alkaline phosphatase in Example 3 are non-elected inventions and have been withdrawn from the examination (see previous office action). Similarly binding protein calmodulin described at page 6 of the specification is also a non-elected component and have not been examined in the current prosecution. Also it should be noted here that Beta-lactamase is inserted into the loop site between 172 Gln and 173 Asp of GFP, and further the specification indicates that the fluorescent intensity of GFP was increased by binding the sensor protein with Beta-lactamase inhibitory protein (BLIP). Specification fails to describe a specific position on GFP sequence where the binding protein Ah receptor is inserted to generate a measurable signal. In Example 3 the specification has not provided the position in the reporter protein alkaline phosphatase where the binding protein Ah receptor is inserted. Therefore, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Further, Applicants have stated that the specification also demonstrates that a sensor protein can be formed by inserting **any** binding protein into a fluorescent reporter protein, such as GFP (page 8 and Fig 7). In response Applicants should note that the Fig 7 is a conceptual diagram, which does not demonstrate any factual data in support of a sensor protein having **any** binding protein inserted to a reporter protein GFP.

Further, the references Tucker et al and Collinet et al submitted by Applicants together with Baird et al (IDS Ref AQ, submitted earlier) in support of the enablement have been reviewed, however, none of the references have described any sensor proteins, having a fragment of a binding protein fused to a mutant of a reporter protein. The reference Baird et al. describes a sensor protein comprising full length binding protein calmodulin (abstract and page 11244, col 2) and reporter protein GFP and mutants thereof. However Baird et al. fails to provide a fragment of binding protein (Ah receptor) as claimed in the instant application. Therefore, references Tucker,

Collinet and Baird do not demonstrate the full enablement of the claimed invention thus the 112, first paragraph (scope) rejection is not overcome.

Conclusion

No claims are allowable.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Jon Weber, can be reached at (571) 272-0925. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette,1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.

Rita Mitra, Ph.D.
July 23, 2004

Supervisory Jon P. Weber, Ph.D.
Primary Examiner